An Improved, High Yielding Synthesis of DMT
Reductive Amination of Tryptamine with $NaBH_4$ and (Para)formaldehyde at a scale of 70 – 100g +

Preface
Fresh on the heels of a minorly successful synthesis of 5-MeO-DMT, written below is one for DMT. The same methodology was employed, but with minor fixes, with an aim of trying not to screw up. There is some optimization but further optimization is always possible. Cooling was with an acetone – dry ice bath. Could be that a freezer would not have enough cooling power for these larger amounts, but really, a dry ice bath doesn't present much of a problem.
The result this time was a unanimous success, close to a standing ovation, a black tie and tuxedo finish. So here we go once again.

Chem info:
Tryptamine (T, 3-(2-Aminoethyl)indole) $C_{10}H_{12}N_2$, Mol. weight: **160.22 g/mol**; Melting Point: **118 °C**; Very soluble in acetone, alcohols; insoluble in chloroform, water (negligible).
Appearance: white to light sandy tan needles or powder.

DMT (N,N-Dimethyltryptamine, 3-[2-(Dimethylamino)ethyl]indole) $C_{12}H_{16}N_2$, Mol. weight: **188.269 g/mol**, Melting Point (freebase): 45-46 and **57-58 °C** (polymorphic, dmt-nexus.com), . pKa: 8.68, Soluble in: chloroform, ethyl ether, dichloromethane (DCM), acetone, methanol, ethanol, MEK, MTBE; insoluble in water. Soluble in naphtha, hexane, heptane but almost insoluble in these solvents at freezing temperatures. Hexane/ naphtha (60 – 80 °C, heavy?) /Pet ether are commonly used to crystallize it and also heptane.
Appearance: white/ transparent crystals or clear oil, darkens on exposure to air.

Formaldehyde (methanal) CH_2O, Mol. weight: **30.026 g/mol**, colorless gas
paraformaldehyde $(CH_2O)n$ is formaldehyde in a polymer, in a chain of 8 -100 units long, one must depolymerize to formaldehyde before using it, calculate molar mass like formaldehyde. White powder, or granules, mild odor of formaldehyde
formalin is an aqueous solution of formaldehyde and could be stabilized by methanol. Sold in various concentrations, 10, 20, 30%, etc. or a max of 36 - 38 % (by weight), calculate for the molar mass of formaldehyde in solution. Density: 1.08 – 1.09 g/cm^3

Sodium Borohydride ($NaBH_4$): Mol. weight: **37.83 g/mol**, white powder/ crystals, hydroscopic, forms a cake exposed to air

Acetic acid (glacial acetic acid, GAA): Mol. weight: **60.052 g/mol**, density of liquid form: 1.049 g/ cm^3, colorless liquid
Sodium Hydroxide (lye, caustic soda, NaOH): Mol. weight: **39.9971 g/mol**, white, opaque crystals **Sodium** (Na): **22.99 g/mol**, 0.9688 g/cm^3, silvery white metallic solid
Methanol (CH_3OH, abbreviated as MeOH): boiling point: 64.7 °C, density: 0.792 g/ cm^3, colorless liquid

Chloroform ($CHCl_3$): boiling point: 61.15 °C, density: 1.489 g/ cm^3 (25 °C), colorless liquid, "sweet, minty, pleasant smell". Often stabilized with ethanol or amylene
Dichloromethane (CH_2Cl_2, abbreviated as DCM): boiling point: 39.6 °C, density: 1.3266 g/ cm^3, colorless liquid, chloroform like smell but fainter
Methyl *tert*-butyl ether ($C_5H_{12}O$, abbreviated as MTBE): boiling point: 55.5 °C, density: 0.7404 g/ cm^3, colorless liquid with a sweetish petrolic smell.
Heptane (C_7H_{16}, n-heptane): boiling point: 98.38 °C, density: 0.6795 g/ cm^3, colorless liquid with a faint petrolic odor.

Part 1: Purification of discoloured, and impure tryptamines

As with 5-MeO-Tryptamine, purification could be an important step to guarantee a better yield of the final product. We use a simple acid/base extract with a DCM "wash".

In this case we begin with **75.983 g** of a fine sandy coloured powder of what is assumed to be **tryptamine freebase**. Calculate as **0.474 mol**.

1) A **1.02 mol equivalent of GAA** to tryptamine is 0.4837 mol or 29.05 g or **27.7 mL**.
In a 1 L beaker prepare a 5% (dilute) solution of acetic acid from the GAA with ~ 550 mL dH_2O.
In a 2 L beaker pour maybe 300 mL dH_2O onto the tryptamine powder and then pour in the dilute acetic acid. I add maybe 4 mL more GAA to lower the pH to 5.3 (measure with a pH meter), but maybe this is not needed, or lower pH to just below 6. Mix on a hotplate/ magnetic stirrer with gentle heating to dissolve quicker. But it could be that this is too much water to use.

2) Will clean the tryptamine with **500 mL DCM** in a **2 L separatory funnel**. Pour in the DCM and mix the layers making sure to vent early on. The DCM collects some colour and some solid mass appears which clings to the sep. funnel. Discard the DCM (bottom layer) and as much of the dark solids as possible. Collect in a waste bottle. Could be that this much DCM is not needed to wash.

3) Pour into a pyrex dish set on the hotplate, heat to 60 - 80 °C, the DCM slowly bubbles off. When most of the DCM has bubbled off, when very little scent of DCM is left, gravity filter back into a 2 L beaker. Use a large medium-speed filter paper folded into a flute held in a funnel.

4) Prepare **19g NaOH** in **600 mL dH_2O**. Pour some water in, dump in the lye, then pour water up to 600 mL, mix with a spoon. Mixture heats up.

5) Once the lye water cools a bit, pour into the tryptamine water. Can pour all or monitor the pH going along. At about ~ 9 pH, a mass starts to appear. Formation of the mass stalls even with large additions of the lye water at 9.6 pH. With the total addition of the lye water, the pH rises to 10.1. Decide to add ~ 3g more NaOH. Prepare 5 g in 100 mL dH_2O. Of this add maybe only 1g in total as the pH quickly rises to 10.3. I think that you really don't need to add much more NaOH than the molar equivalent to tryptamine. Works out to about **17g**.

6) Set up a smaller Büchner funnel (one that holds 110 mm filter paper) over a 2.5 L vacuum flask. Under vacuum pour onto a well-adhered, damp medium speed filter paper. Any amount more than this, I would use a larger size Büchner funnel (with 240 mm paper).

7) Air dry with a fan blowing intermittently in a crystallization dish, but to fully dry it takes a long time, overnight, and the next day. Could have run it under vacuum for a longer time. Sift the powder to check whether it is still pasty (damp) and whether it adheres to the bottom of the dish. Once fully dry, collect **70.762 g** of a pale sparkly tryptamine powder (**0.442 mol**) or a 93.2 % "yield". The colour and appearance are very pleasing.

Part 2: An improved reductive amination of tryptamine to DMT in the springtime

The plan is to run the reaction slightly different than the previous one for 5-MeO-T, as there will be no heating between cycles and instead of 4 cycles, 5 are planned. Also, I will monitor the reaction at the end of each cycle on TLC plates to see how much tryptamine (if any) is left.

Otherwise roughly the same amounts as when working with 5-MeO-T, a **2 mol eq**. of **formaldehyde** for **cycle 1**, for **cycles 2 – 4**, a **1 mol eq.** *from the mol tryptamine* amount. For **cycle 5**, the amount of formaldehyde will be decided based on TLC (thin-layer chromatography). The **$NaBH_4$** amounts for cycles **1 – 4 are 0.6 mol eq**. *from the mol formaldehyde* amount for that addition (cycle). **One hour** between adding the $NaBH_4$ and adding the next formaldehyde. The amount for the last addition will be decided based on TLC as well.

Information on TLC, An Interlude to Part 2

For the TLC I followed a method that Sawdust and Honey on The Vespiary forum developed for tryptamines:

From *https://www.thevespiary.org/talk/index.php?topic=16470.msg54205305#msg54205305*

"I used the same 1mm/80mm capillary tubes I use for melting points. With the compound concentration I had (50mmol in 250ml methanol), the mixture itself was a bit too conencetrated. So what I did was take up 2-3 drops of the reaction mixture and dissolve it in 3-5ml methanol.
A TLC starting line was drawn with a pencil (be careful not to scrape down the silica) and a very small, 1 (only one!) spot was done of each reaction mixture and solution of tryptamine in methanol (conc. very small too, I can't lie to you, I just eyeballed a couple tens of mg of tryptamine and dissolved it in 10ml of methanol and used it as a standard in all my TLCs). You should use a 254nm UV lamp, don't bother with KMnO4 or iodine. UV is MUCH, MUCH cleaner and non-intrusive. Just make sure that your plates are covered with F254 or something similar. They should be greenish, while the surroundings in UV are violet/blue. You'll see whether the spot is concentrated enough if the spot is well-visible and small in diameter. You will also need to adjust your concentrations a bit with experiments, if you're getting smeared results then the concentration is too small.

The eluent used was 10:0.5:0.5:0.25 volumetrically ethyl acetate:methanol (ethanol works too):n-hexane:25% ammonia. Realistically I recommend doing 10 drops of ethyl acetate to 1 drop of everything else. Or you can just make up some of the eluent, it's generally useful for tryptamines. N-alkylated tryptamines tend to be less polar and therefore climb higher on the plates."

First I prepared the tryptamine standard that I would spot on all plates, dissolved about 10 – 13 mg of the cleaned tryptamine in 5 mL MeOH and set that aside in a small beaker.

The eluent that I mixed up was 10 mL ethyl acetate with 0.5 mL MeOH, 0.5 mL hexane, and 0.25 mL 25%

ammonia. However, I tweaked the mixture over the course of the reaction and found that a mixture with **10 mL ethyl acetate, 0.8 mL MeOH, 0.5 mL hexane, and 0.5 mL 25% ammonia** was better, spots would travel further. Believe this made the mobile phase, or eluent, more polar. With an increase in the ethyl acetate proportion, the spots stayed on the bottom and a clear reading was not possible.

However to better compare plates during a synthesis you shouldn't change the mixture. Mix up a larger amount and use the same mixture on all plates.

As for the **hardware**, the TLC plates were the cheap **25 x 75 mm** size ones from AliExpress. **GF254** type **silica gel plates**. You can find them on amazon for slightly more as well. They were perfectly adequate for the job, just need to be a bit careful as the silica crumbles off easily. But they are totally fine.

Once the spots dry, they are only visible under UV light, so to visualize, a **handheld UV analyzer** was also bought from AliExpress. The one with a **254 nm and a 365 nm switch**. Not only are they perfect for visualizing plates in the dark, but you can also grab a sheet of acid, lock yourself in a dark closet, turn on the lights (UV), and just watch the sheet glow. Very easy to see whether a sheet of acid has been layed well. These analyzers work much better than UV flashlights, and I think they come out cheaper than booking a place at the local nail salon each time you lay acid.

In the past, whenever I would go out to get my nails done I would also bring along a fresh sheet of LSD. After some rigorous nail grooming when it was time to check out those beauties, I would bust out that 30 x 30 tab sheet and stick it under the nail light to analyze how even the drops were. In the nail tavern this always attracted the odd stray glance, and a few uneasy questions.

These portable UV analyzers are such a fortuitous discovery! No longer do I have to kill two birds with one stone, now I can just let my nails grow unkempt and hideous. These homebound UV analyzers will put every nail salon out of business! And there is even a portable version, so I can check my nails on the go as well!

Ok, back to the TLC. To create a TLC developing chamber use a 250 mL beaker. Pour in the eluent you have prepared. Take one of your round 110 mm filter papers and cut off 1/3rd. Stick it curved to the wall of the beaker so that it is maybe a few cm off the bottom, but the top doesn't go above the top of the beaker. It doesn't have to soak up the eluent now. The plates will suck up some of the eluent and some will evaporate as well, the ~ 12 mL might just be enough for 5 plates.

Keep the beaker covered with cling film, parafilm, or a watch glass, the mix evaporates and also the ammonia and EtOAc makes the mix a bit stinky.

To first test out the plates, I took a drop of the tryptamine standard with a 2 – 20 µl micropipette which I set to drop size 1.5 µl. Can use a flimsy capillary stick as well, but I did it the cool way (also have micropipettes on hand).

On the bottom of the plate carefully draw a line 1 cm from the bottom with a soft (4B) pencil. Drop the tryptamine standard on the line maybe 1/4th way from the left edge (will be making a few lanes on the plate so this is a good way to practice). You can also label the lanes with a pencil below the starting line.

Wet the filter paper by swirling the beaker now so that fumes saturate the beaker (chamber).

Now wait a minute or so for the methanol to evaporate, and with tweezers grab the very top of the plate and place it vertically in the beaker.

It is off to the races! Quickly the mobile phase travels up the plate, in maybe 2 to 3 minutes it will be near the top, so when it is about 0.5 cm from the top, grab it with tweezers and set it on a watch glass or somewhere to fully evaporate, but quickly before the eluent starts to disappear from the plate, mark the solvent line. Let the plate stand for a few minutes while the solvent evaporates off some more.

Now we can visualize in the dark. And if we measure the proportion the spot travelled from the starting line to the solvent front, we can calculate a retention (or retardation) factor value specific just for this particular compound in this particular eluent mix.
In this case the tryptamine traveled 1.2 cm from the starting line of the plate to the center of the stain seen under UV, the solvent front travelled 5.6 cm until it was removed from the developing chamber. Since $\mathbf{R}_f$ = distance travelled by the compound/ distance traveled by the solvent front, 1.2/ 5.6, this gives a $\mathbf{R}_f$ of 0.214.

Again, there is a good guide here:
https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Organic_Chemistry_Lab_Techniques_(Nichols)/02%3A_Chromatography/2.03%3A_Thin_Layer_Chromatography_(TLC)

Intermission Over, Back To The Second Part of Act II

The main improvement in this synthesis is that **no water** will used, in fact it might be better to dry your MeOH beforehand, but for this run I used fresh 99.5 % general purpose methanol. Instead of formalin we shall make a **30% solution of formaldehyde in MeOH**. By keeping the reaction dry it pushes the equilibrium forward (it is a reversible reaction) and it seems that it helps with both the yield and the quality of the final product.

To make the methanolic formaldehyde solution, **sodium** will help to dissolve **paraformaldehyde**.

1) Again calculating for the total amount of formaldehyde we will need in the reaction: If we start with 70.752 g tryptamine (used 10 mg for the tryptamine standard) (0.442 mol): cycle 1: 0.884 mol or 26.543 g CH_2O, cycles 2 – 5, 0.442 mol or 1.768 mol or 53.068 g or a total of about 79.63 g, we shall take a slight excess of this (x 1.05). The total amount is 83 g of para(formaldehyde). This is calculating for a 5^{th} cycle of 1 mol eq. which we probably won't use. But an excess is a good thing.

2) A 30 % solution would be **83 g of formaldehyde in 275 mL MeOH**. The paraformaldehyde has no chance of dissolving in the methanol, but with sodium metal, it will help to depolymerize it.

3) With a scalpel cut off small pieces of Na, dry them with a paper towel (if it was dipped in paraffin in the storage container) and weigh out the dry Na in a petri dish. For this amount we need 400 – 420 mg **(210 mg paraformaldehyde/ mg Na**). Transfer to a toluene bath in another petri dish. If not in pieces, cut with a scalpel into maybe 3 chunks. Dry with a paper towel again (with gloves on) and under magnetic stirring flick it into the methanol, there is some hissing and the sodium dances on the surface of the methanol, maybe there is even smoke if throwing in a larger piece. But not a cause for worry.

With sodium additions, the paraformaldehyde depolymerizes, turns into formaldehyde and dissolves into the methanol. Bit by bit the paraformaldehyde disappears. However, at a certain point I notice that

even with further Na additions, I could not get a completely clear MeOH layer this time. Do not know what caused the faint wispy, milky cloudiness left. Do not think it was undissolved paraformaldehyde, maybe something different, some possible impurities. Whatever it was, the cloudy layer sank to the bottom when nothing further was dissolving.

Kept this in mind during formaldehyde additions as I decanted into a small beaker, being careful not to pour the bottom layer.

Cover the mixture, it has a faint whiff of what I assume to be CH_2O, but nothing overpowering.

A bit later decide to test the pH of the solution and it reads a high 11.3. So I add a few or 4 mL GAA to bring it closer to neutral, but at some point I overshoot, and the **pH** of the methanolic solution ends up as **6.7**. This is an important consideration, and it could be a minor discovery.

The acidic pH could have made some difference in the course of the reaction. As $NaBH_4$ tends to react much quicker in acidic conditions. Maybe it even helped the reaction along? Next time I will try to aim to lower the pH close to 7, but not below it, and see if it makes a difference in the tempo of the reaction. And likewise, maybe there will not be much of a difference whether the pH is high or slightly acidic.

4) In a beaker dissolve the tryptamine in <10 mL MeOH /g tryptamine. I use maybe 720 mL for the 70.752 g tryptamine, and this was too much. You could get away with 7 mL MeOH for every gram of tryptamine, there is a report of bulk production using 5 mL to 1 g. There is just no need to use 15 mL/g or larger amounts like in other reports. This might make the difference between vessel sizes when working with a larger starting amount of tryptamine or 5-MeO-T. In a 2 L flask, if filled up to 1.2 L max, you could risk 170 g, now I am not sure how feasible this is as during additions things start to fizz somewhat, larger additions, more bubbling, this could result in an overspill.

But it is entirely possible to react **100g** of either tryptamine or 5-MeO-T, in a **small 2 L flask**. Desktop size in a small fume hood. Just imagine that! Now imagine working with an equivalent amount of bark. 5 to 10 kg, and now we can see what we are getting at…

In general tryptamine dissolves very well in methanol so next time I would lower the **methanol amount to 7 mL/g**.

5) Pour the dissolved tryptamine into a 2 L 3-neck round bottom flask. One neck has a thermometer, another neck is stoppered, the centre neck will be mostly stoppered; except during additions when I use one funnel for $NaBH_4$ additions, and one for formaldehyde additions (pure $NaBH_4$ can react strongly with streaks of formaldehyde on the funnel, so use two separate ones).

6) Prepare an acetone – dry ice bath in a cylindrical glass dish. This does not need to be some fancy giant lab crystallizing dish but could be a giant vase, you can find these for decent prices on amazon. To err on the safe side, let's purchase 5 kg of dry ice. If it sits out overnight or longer and some sublimates away we should still have enough working at this scale.

It might be wise to crush the dry ice between towels into smaller chunks or even a powder, so it does not boil so much with additions.

Fill the glass dish with a layer of crushed dry ice on the bottom.

Fill a plastic wash bottle (or an old bicycle water bottle) with acetone and squeeze *slowly* onto the dry ice. DO NOT pour acetone on the dry ice, I have cracked such a beautiful glass dish in my last synth this way. The dry ice fizzes and CO_2 is given off, the acetone bubbles. The dry ice might jump around so violently that it breaks the dish, so first just wet the dry ice with acetone, continue squeezing on the wash bottle to submerge the dry ice somewhat, and only then start freely pouring the acetone.

Fill the glass dish with maybe 2.5 L acetone (of course all depends on the size of your dish) but maybe to what would be a bit below the level of the methanol in the RBF.

7) Fit the flask into the larger cylindrical glass dish, and squeeze that into a makeshift Dewar container made out of a hole cut into two layers of styrofoam, and place all of that onto a magnetic stirrer. For this amount I think magnetic stirring is sufficient, when moving to 5 L or 10 L flasks, would probably use overhead stirring. Stir at a decent clip with an egg bar, at 500 RPM for the duration of the reaction.

Wait some and watch as the temperature drops. Now my thermometer only registers to −10 °C, so keep in mind that a better thermometer for this particular reaction would be a −50 to +50 °C one.

Aim for an internal temp of −25 °C or even lower for the first addition.

8) For the first addition and the first cycle, again, we add **26.54 g CH_2O** or **87 mL of the 30 % solution**. Add all at once, there should be no change in temp for now. After about 10 min, start to add in portions the **20.046 g $NaBH_4$**. Add maybe a few, maybe 5 g of the boro, even this amount, not all in one pour. Notice some fizzing start, maybe there won't be much bubbling for now if the temps are still very low, but the temperature will certainly soon rise. There might be a bit of a delay in the temp rise as the boro takes its time to explore and swim around in its new home. Hydrogen gas is released so make sure there are no open bonfires around and that your environment is free from sparks.

UNDER NO CIRCUMSTANCE pour in all of the $NaBH_4$ at once or even in 2 large portions espaced by a minute. You need to watch hydrogen evolution, watch the temp, and really get a feel of what is going on. Add the $NaBH_4$ *slowly*, the first addition is the most important and the most reactive, and it could take a full **15 min of delicate additions** to keep the temperature under −5 °C.

You are a cook, so imagine that you are Gordon Ramsey putting the finishing touch on the filet mignon, just that perfect sprinkle of salt on the marbled chuck of Kobe beef. We do not want a spectacle like that of Jamie Olivier throwing Himalayan rock salt blindly behind his back into a Caesar salad bowl with limp chunks of chicken. Do you remember how that ended? Everyone shat themselves in yoga class.

And how did I go about things? Added far, far too quickly. When the temperature started to rise, it showed no signs of stopping to my terror. It could also have been that the dry ice bath was not sufficiently deep enough, and I might as well have rushed, could have waited some more for the bath to cool down further.

I quickly reach for more dry ice to add to the bath, also pour in more acetone. The reaction mixture is really fizzing, and bubbling strongly now. It is I believe at temperatures above −5 °C when the boro really kicks into action. So if the RM is cold all the time, the boro is mostly dormant or held at bay.

The RM temp shoots all the way to 20 - 22 °C and I am certain the entire experiment, the entire batch, is ruined. But the addition of fresh dry ice kicks in and the $NaBH_4$ bubbles away fast, so the temp drops

almost as quickly as it rose. The RM did not spend much time at high temps, but some damage must have been done; a portion must have underwent Pictet-Spengler reaction conditions to form god knows what sort of atrocious β-carbolines.

You must place your mind in the contraption, your mind must reside within the flask, and be just as cool as the dry ice.

Imagine the story of the world reflected in this reaction, the battle between good and evil fought out, between energetic hydrogen and heat evolution, and the dry ice trying to put its icy shackles down, trying to tame the wild and youthful $NaBH_4$…

9) Once the $NaBH_4$ addition is complete, and the temp has settled down (and is down on the bulb) and you have settled down, start a timer for **1 hour** and settle in. But one can take an additional step, and an additional step towards perfection, once you see that hydrogen gas evolution has really slowed, you can spray the flask with preferably argon gas, or nitrogen from a tank. If gas evolves it might just burp a stopcock, or it could fly off into the bath, the worst that could happen. One could use a septum punctured with two needles as well, in that case H_2 would escape but outside air wouldn't get in, but I was too lazy to use a prophylactic this time. Just squirt raw argon into the flask before quickly stoppering.

10) Once 40 – 50 minutes have passed, you could prepare the first TLC plate. So I decide to make 3 lanes. The left most lane is the tryptamine standard, the middle lane is a co-spot of both the reaction mixture and the tryptamine standard, and the right lane is just the reaction mixture. The co-spot might help to better visualize, and help to compare with the reaction lane, or it could serve as a dual control lane. Could help if there are ambiguities in determining the product when there are very similar spot between product and reactant.
So imagine the TLC as 3 parts, in the middle of each part is where you should place the drop on the 1 cm line. Label however you want the lanes, Schumacher (Sc) or Hamilton (Ham), what do I care? You can live out whatever fantasy you want in your little TLC world. And just like in a perfect world, at the end of the race, there will be only one clear winner (a single clear product spot), two clear second places (the co-spot has a clear product and a clear reactant), and the loser is on the podium as well, clearly. Outsiders might appear in the field. That would be cause for concern, as these unofficial racers were not there at the start, so how did they sneak into the finish?

BUT we want to prepare the tryptamine spot only shortly before the Co and the Rx spots. All three should evaporate at about the same time. Take a reading at the end of the one hour cycle before the second addition.

As well, to keep ourselves busy, we can weigh out the boro and set aside the correct amount of CH_2O for the second addition, **44 mL of 30 % formaldehyde** and **10.036 g $NaBH_4$**.

11) Back to the TLC front.
Now to take an aliquot for the reaction spot we use a plain 5 mL pipette fitted with a scroll wheel to draw up a small amount of the RM. Into a petri dish, drop in with the slightest back scroll a single drop of the RM. Dilute this **drop with 1 mL MeOH** that we draw up with a 2 mL pipette from our MeOH bottle or canister. Mix the RM drop and MeOH a bit. Could also use 3 drops of the RM to 3 mL MeOH. Only then do we use the micropipette to draw up a **1.5 µL drop**. So two drops of the tryptamine control: one on the left and centre lanes, and two drops of the RM: one on the center on top of the tryptamine and

one in the right lane. Remember to use new pipette tips with each new plate, and also thoroughly clean the pipettes. We do not want to contaminate results.

The spots evap some, and maybe we can even drop in the formaldehyde if an hour is up. Place the plate into the TLC tank for elution.

Now something curious occurred, the temperature rose with this second formaldehyde addition, this could mean that there was $NaBH_4$ it was reacting with from the previous addition, or it could be just the CH_2O reacting, doing its bit in the first imine formation. Wait for things to stabilize, wait for those few minutes before $NaBH_4$ addition. Do another round of slow boro addition, try and keep the temp under −5 °C. However if temps skyrocket to 10 °C or whatever for a short bit, it really is not the end of the world. As the reaction is mostly water-free, I think this helps to safeguard against that evil of evils – Lords Pictet-Spengler.

Our TLC plate has been pulled out in the nick of time. It was about to drown in methanol but you saved it from a horrific fate of blind readings. Draw the line as soon you have set the plate down. Let the plate evaporate for a minute or two, and now we can head to our darkroom for a moment of fun.

12) Now put on those stunna-shades 'cuz we bout to twerk. Oh precious UV rays you show me the world, but you blind me as well. Uhh wee!

Under UV also mark the spot stains lightly so you can measure their distance travelled accurately with a ruler. After an hour of reaction time the TLC in Rx shows two spots: a big lower one with an $\mathbf{R}_f$ of 0.084 and a pale upper one with a $\mathbf{R}_f$ of 0.258, so we need to keep on moving along.

13) The **3rd addition** is much like the 2nd, after CH_2O addition the temp rises all the way to 10 °C, cool quickly but at this point not much dry ice is left.
The second TLC shows the tryptamine lane with a $\mathbf{R}_f$ of 0.057, and the reaction lane with two spots again, one spot similar to tryptamine but paler, with an $\mathbf{R}_f$ of 0.065 and a more bright top spot, with an $\mathbf{R}_f$ of 0.262, the co-spot is similar to Rx, but the tryptamine spot is brighter. So it could be a portion of the tryptamine has reacted, but some remains. At this point I add ethyl acetate to the eluent as the lower spot was too low for my liking.

14) 4th addition goes ok, temps not too high, but I run out of dry ice (used maybe 2.5kg), run TLC for the third time, and the spots are way too low, cannot interpret measure the distance properly and interpret that data. Turns out I needed to add more 25 % ammonia sol., not EtOAc. Mix up a fresh batch of eluent and in the beaker put in a fresh filter paper.

15) After the **4th cycle** finishes, take a TLC reading for the 4th time, and it turns out very well. Tryptamine shows the faintest of spots in the reaction lane, but still some remains, so I go for a 5th cycle.

16) The **5th cycle** is run with a small addition of both the formaldehyde and the $NaBH_4$. For no good reason decide on a **0.5 mol eq. of CH_2O** and a **0.5 mol eq. of $NaBH_4$** from the mol amount of CH_2O. So 0.221 mol (**22 mL formaldehyde** solution), and 0.1105 mol $NaBH_4$ (**4.18g**). Add plain ice and run the reaction until the ice melts and everything fizzles out. At some point take the last (5th) TLC plate and it looks good as well, but I dropped spots twice (believe the reaction aliquot was too dilute) so have some difficulty interpreting whether it was ghosting, or did another product appear from a side reaction?

Seal the flask with argon gas and leave overnight.

17) In the morning notice that there is precipitate in the flask already. Maybe this is DMT but could as well be an unwanted product. Pour the RM into a one neck RBF to distill off the MeOH.

Part 3: An Improved Work-up Of The Reaction

Now the plan is to get rid of a larger portion of the MeOH, dilute with water, extract with chloroform, get rid of the chloroform, extract with MTBE and precipitate the DMT with heptane addition. There will be no addition of sodium or potassium carbonate, just plain water. Instead of using DCM we shall use chloroform as DCM reacts with DMT (abeit slowly) and also DCM forms emulsions during the first few extracts which are to clear up.

In fact, thinking now, maybe you could just replace the chloroform with MTBE?
And by dissolving in the smallest possible amount of MTBE, I could crash out DMT crystals with the smallest possible amount of heptane? We shall see if it works.

1) Set up for vacuum distillation, use a 2 L heating mantle with magnetic stirring, grease all the joints with vacuum grease, flow cold water through the condenser and set the receiving flask in cold water as well. I do not have the best vacuum source, a diaphragm one, but it manages to boil the MeOH at somewhere around 36 °C. Could have been higher though as the heating mantle shows a lower temp, but this time the seals were much better. It is important to use the correct grease it turns out.

Distills well, collect **610 mL MeOH** which is clean enough to re-use for next time. Have this thick yellowish mush, there is residual MeOH in there, but it didn't seem to cause any further problems.

2) Dilute the yellow mush with **500 mL dH_2O**. I take the pH of the mixture and it is a high 12.4. Speculate that adding K_2CO_3 would not do anything so will extract with chloroform now.

3) Transfer the mixture to the 2 L sep. funnel and pour in 100 mL chloroform. Make sure to wear a mask around chloroform or work with it under good ventilation.
Mix the two layers very thoroughly and notice straight away that chloroform separates easier than DCM, For the 2nd extraction use 80 mL chloroform, the 3rd use 70 ml, 4th and 5th 50 mL each. Used about 350 mL chloroform, but the beaker shows a higher level as there is DMT in there! The layer is a darker yellow and not entirely clear because there is water in there as well which we need to get out.

4) At 20 °C chloroform can hold 0.81 g of water/ 100 g. So about 4.22 g of water are dissolved in the chloroform. Magnesium sulfate ($MgSO_4$) can absorb 0.15 – 0.75 g water per g. If we take 0.5 g, then need 8.44 g of $MgSO_4$, if 0.15 g, then 28 g.
Decide on another extract of 75 mL, pushing the total amount of **chloroform** to roughly **475 mL**, roughly 5.72 g water dissolved in the chloroform then, but I calculated the water amount wrong, and use 6 g $MgSO_4$ that I stir in.
Under magnetic stirring, add an additional 2g. Quickly the chloroform clears up to reveal a crystal clear piss-golden layer. Add some more $MgSO_4$ until it no longer clumps and is truly free flowing. Now the layer should be dry.

5) Try to vacuum distill the chloroform in a smaller 1L RBF, but it does not go well. As with DCM, the chloroform seems to boil but it does not condensate well in the receiving flask, drips slowly, and I do not want to add more heat, and a lot is travelling through the pump into the room. So I shut off the system and decide to evaporate the chloroform the old-fashioned way: in a pyrex dish set on a hotplate. To properly distill these volatile compounds you need a deep vacuum, with traps. A 2 stage rotary vane pump. One of those heavy Leybold Trivacs or Edwards.

With a fan blowing and the hotplate set to 60 °C, the chloroform easily evaporates off in the fume hood.

6) Transfer the thick sticky orange sludge to a beaker to weigh, when it cools it begins to crystallize, very promising! The weight of a 250 mL beaker is 100 g, tare and the sticky layer weighs 85.35 g, I have a feeling that this is mostly DMT, could also be some residual chloroform left.

7) Now I followed this patent for 5-MeO-DMT recrystallization:
https://patents.google.com/patent/EP3753923A1/en

Decide to use a 0.7 equivalent of MTBE by volume, so 60 mL to dissolve the crystals/ sludge. Heat up the mass and MTBE to 50 °C, with stirring everything dissolves well. Cool the mixture to room temperature and the MTBE stays liquid, pour into a pyrex dish and squirt in some room temperature heptane. Some white wisps appear but they quickly disappear. Pour in the rest of the heptane for a total of 60 mL and set in a freezer. Can see that nothing is happening and that nothing will. The method just did not work.

Return the plate to the fume hood, and on a hotplate evaporate off most of the heptane and the MTBE with gentle heating. As a portion evaps off, the mass starts to crystallize, so it could be that I used too much MTBE to dissolve. When most seems to have evaporated off, once again scrape off the sludge, and return to a 1 L beaker. Hey! This really looks and smells like DMT now! Still there are impurities to be rid of.
So we are moving on to a tried and true method, hot extraction with that lovely, lovely ***heptane***.

8) Ah I love me heptane, my favourite straight-chained alkane. It has a mild and pleasant odour, and it is relatively non-toxic. As well it's not as volatile as DCM or hexane, and has a sane boiling point. A pleasure to work with, I should write a sonnet about and on heptane one day.

On a hotplate with magnetic stirring heat the beaker with the *crude* DMT to 65 °C so that it readily melts and turns into a free-flowing liquid, could keep the heat at 60 °C as well.

9) Do a classic hot heptane extraction, similar to any other re-x of DMT. What is in the beaker should be mostly transferred to a pyrex plate for crystallization, with each extract the product in the beaker gets smaller and smaller, until all that is left is a sludge of impurities that heptane will not extract, as it is not DMT. In this regard heptane is very specific, it will not pick up anything else in the reaction. Just DMT, seems to be even better than hexane in crystallizing out only beautiful white crystals.

As the red-yellow-orange oil is stirring away, in the heating mantle heat up 100 mL of heptane until it just about boils. Pour into the beaker with the DMT, and mix furiously. The heptane becomes cloudy white, decant quickly into the pyrex dish set next to you. But be very careful not to decant the lower layer. You will repeat this process as many times as it takes until only the sludge is left.

Extract a total of 8 or 9 times 100 mL each time. The last extract when almost nothing was left was 50

mL heptane. Could have used almost **a liter of heptane**.

As the pyrex plate cools amazing crystals form, you pour fresh hot heptane in and it clouds up, only to later reveal more beautiful crystals. The process is straightforward enough, just don't get any of the bottom layer in, you will pour more heptane on top in the next extract, so it doesn't matter that you didn't decant everything.

10) Let the plate cool to room temp and let it stand an hour or so until the heptane layer is clear, then transfer to a freezer. Cover with foil or something. According to DMT-Nexus heptane in the freezer will hold 916 mg DMT in 1 L, so there will still be some left in the heptane even after decanting. We are going to get ALL OF IT!

11) The next day open the freezer door to see an even more wondrous sight, the plate just looks stunning, there is a thick mass of crystals. Getting very exciting. Decant the heptane by pouring into a filter held in a funnel over a beaker. Spill a bunch of heptane as the plate was rather full. The filter captures no further DMT as all is adhered to the plate.

Place the plate in a fume hood with a fan blowing on it to completely dry.

12) Now to get all of the DMT we shall distill the heptane, and in the process **re-use** it. No need for vacuum distillation, plain will work, **heptane distills** well, but do run cold water through the condenser and wrap the still head in foil.

Do no collect the first 50 mL or so as it might be impure from having run through a possibly dirty condenser and glassware. Change the collection beaker and collect most of the distillate. Watch closely so that 50 mL remains in the boiling flask, this last bit of heptane will have a bit of color. We are not collecting this. Just make sure not to distill to dryness! Heptane is flammable and there is DMT in there we don't want to burn. The heptane in the receiving flask seems crystal clear, and I judge it fit to re-use. Pour back into your heptane container. There is almost no waste this way. Heptane can be expensive, but we can re-use it many times. Just like with the methanol. So why not just get the highest grade heptane and methanol for your use.

What is in the boiling flask pour into a pyrex dish to evaporate away.

13) Using a razor blade scrape up a whopping 61.552 g of slightly off-white crystals from the pyrex plate. Just unbelievable, it really is a **mountain of DMT**. And this time there is just none of that melted mass stuck to the bottom. It is all solid white crystal corresponding to one polymorph. In the other plate there is about 400 mg with a few impurities that I pick out, I load this straight away into a vape.

It could be possible to use PP plastic crystallizing dishes and maybe the DMT would pop off easily, wouldn't have to scrape. But the compatibility of PP with heptane is listed only as fair, with hexane it is more compatible, so I opt to use glass.

In total collect **61.952 g** of what appears to be **DMT**, from a starting amount of ~ **70.752 g tryptamine**. This works out to about a **74.5 % yield**. Almost perfect.

14) Not quite there still. Let's take the **melting point** of this mystery compound in a Thiele tube with two side-arms. Load the tube with some white mineral oil just above the loop, and fill a melting point

capillary maybe 4 mm from the bottom with finely chopped filet de DMT. Scoop up with the help of a scalpel. Then drop the capillary onto a hard surface through a tube to compact the compound on the bottom.

Clasp the Thiele tube and thermometer in two separate clamps attached to a ring stand. Place the capillary so that it rests against the bulb of the thermometer, and that you have a clear line of sight. Heat the Thiele tube loop with very gentle heat from a Primus stove. Wave the flame around once the temp. goes above 40 °C, making sure it rises very slowly, and start watching the capillary closely. First the sample will sinter and only later will it melt, it can be hard to tell.

Record the moment when it starts melting. The top liquefies at 58 or **59 °C**, and it seems to continue melting until **65 °C** when all of the sample is a liquid. This corresponds to the data found here:

https://wiki.dmt-nexus.me/
Psychedelic_Compounds_Chemical_and_Physical_Properties#Freebase_DMT
and here:
https://www.erowid.org/chemicals/dmt/dmt_chemistry.shtml

Just another nail in the coffin. As with 5-MeO-DMT I noticed that it starts to discolour rather rapidly, after a day it had gained this more distinct crème color. Some light tint of pink/orange/yellow. So it would be wise to transfer the DMT to a clean media bottle, flush with argon, and quickly cap it. Store in a freezer.

After-jibberish
Truly this synthesis turned out to be a great success, so even with large amounts, a yield of over 80 % is entirely possible. Just need to control temperatures more during additions. That is all folks, happy vaping.

Try it, it's really cool!

Fin

Part 4: Visual Addendum

Overview of the reaction vessel, before the first cycle. Another styrofoam layer was added, acetone level too low here

Vacuum distillation of MeOH

Clear layer of chloroform after drying with MgSO4

Raw DMT, before extraction with hot heptane

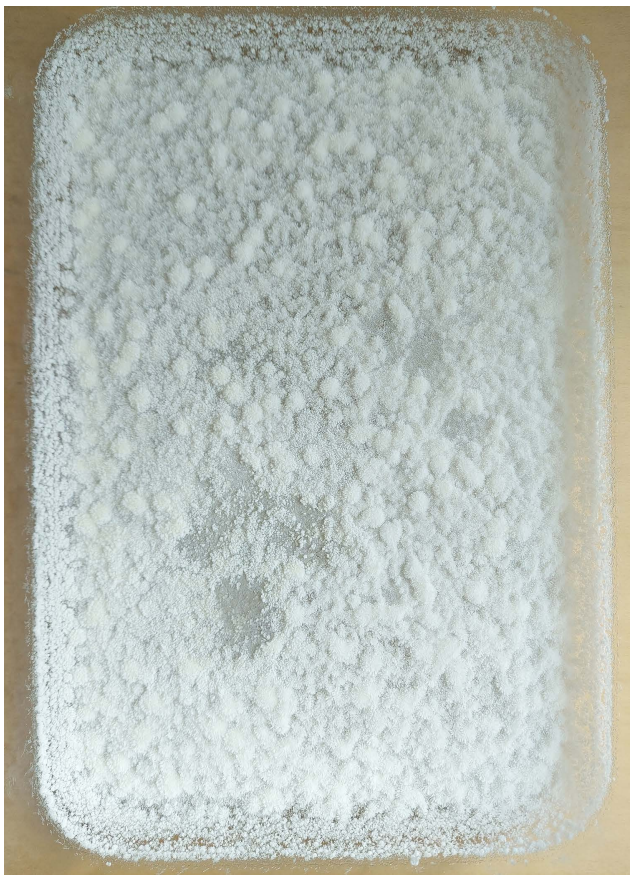

Plate full of crystals, plate of beauty

Determing the melting point with a Thiele tube

TLC plate 1, must have forgotten the T spot, but it is the lower one, shows it is mostly unreacted

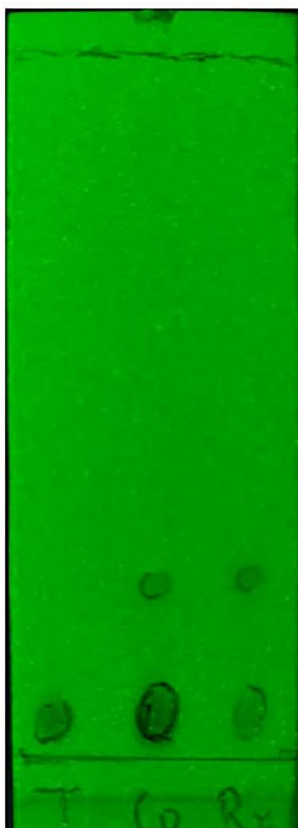

Plate after 2nd cycle

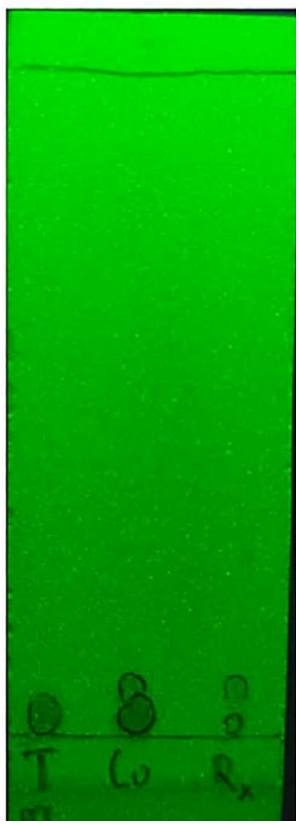

Plate after 3rd cycle. Poor reading

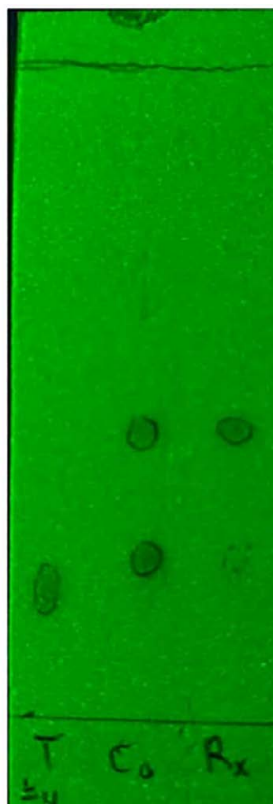

Plate after 4th cycle. Very good

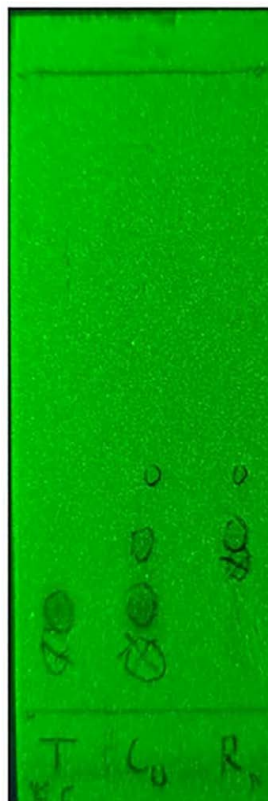

Plate after 5th cycle. Strange ghosting